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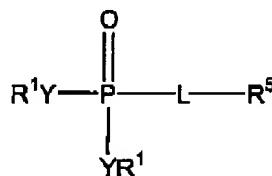
Patent
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AMENDMENTS

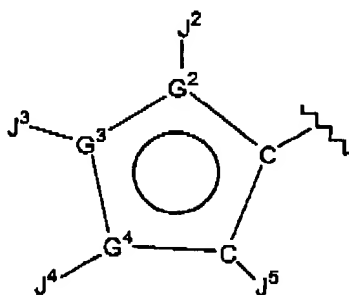
In the Claims

Please amend the claims to read as follows:

34. (Once Amended) A method of treating complications of diabetes or cardiovascular diseases in an animal which comprises administering to an animal suffering from complications of diabetes or cardiovascular diseases a pharmaceutically effective amount of a compound of formula (I):

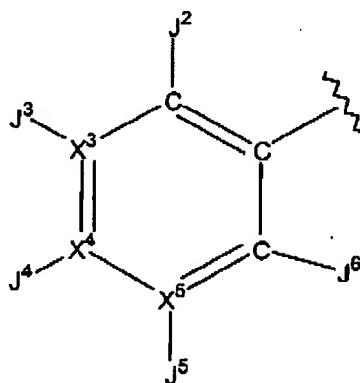


(I)

wherein R⁵ is selected from the group consisting of:

I (a)

and



I (b)

wherein:

G² is selected from the group consisting of C, O, and S;G³ and G⁴ are independently selected from the group consisting of C, N, O, and S;

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wherein a) not more than one of G^2 , G^3 , and G^4 may be O, or S; b) when G^2 is O or S, not more than one of G^3 and G^4 is N; c) at least one of G^2 , G^3 , and G^4 is C; and d) G^2 , G^3 , and G^4 are not all C;

X^3 , X^4 , and X^5 are independently selected from the group consisting of C and N, wherein no more than two of X^3 , X^4 , and X^5 may be N;

J^2 , J^3 , J^4 , J^5 , and J^6 are independently selected from the group consisting of -H, - NR^4_2 , - $CONR^4_2$, - CO_2R^3 , halo, - $S(O)_2NR^4_2$, - $S(O)R^3$, - SO_2R^3 , alkyl, alkenyl, alkynyl, alkylenearyl, perhaloalkyl, haloalkyl, aryl, heteroaryl, alkylene-OH, - $C(O)R^{11}$, - OR^{11} , -alkylene- NR^4_2 , -alkylene-CN, -CN, - $C(S)NR^4_2$, - OR^2 , - SR^2 , - N_3 , - NO_2 , - $NHC(S)NR^4_2$, and - $NR^{18}COR^2$;

L is selected from the group consisting of:

i) a linking group having 2-4 atoms measured by the fewest number of atoms connecting the carbon of the aromatic ring and the phosphorus atom and is selected from the group consisting of -furyl-, -thienyl-, -pyridyl-, -oxazolyl-, -imidazolyl-, -phenyl-, -pyrimidinyl-, -pyrazinyl-, and -alkynyl-, all of which may be optionally substituted; and

ii) a linking group having 3-4 atoms measured by the fewest number of atoms connecting the carbon of the aromatic ring and the phosphorus atom and is selected from the group consisting of -alkylenecarbonylamino-, -alkyleneaminocarbonyl-, -alkyleneoxycarbonyl-, -alkyleneoxy-, -alkylenethio-, -alkylenecarbonyloxy-, -alkylene-S(O)-, -alkylene-S(O) $_2$ -, and -alkyleneoxyalkylene-, all of which may be optionally substituted;

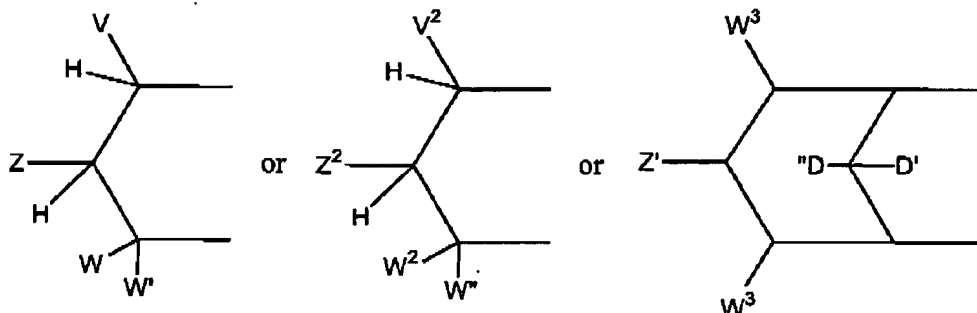
Y is independently selected from the group consisting of -O-, and - NR^6 -;

when Y is -O-, then R^1 attached to -O- is independently selected from the group consisting of -H, alkyl, optionally substituted aryl, optionally substituted alicyclic where the cyclic moiety contains a carbonate or thiocarbonate, optionally substituted arylalkylene-, - $C(R^2)_2OC(O)NR^2_2$, - $NR^2-C(O)-R^3$, - $C(R^2)_2-OC(O)R^3$, - $C(R^2)_2-O-C(O)OR^3$, - $C(R^2)_2OC(O)SR^3$, -alkylene-S-C(O) R^3 , -alkylene-S-S-alkylenehydroxy, and -alkylene-S-S-S-alkylenehydroxy,

when one Y is - NR^6 -, and R^1 attached to it is - $(CR^{12}R^{13})_n-C(O)-R^{14}$, then the other YR^1 is selected from the group consisting of - $NR^{15}R^{16}$ -, - OR^7 -, and $NR^6-(CR^{12}R^{13})_n-C(O)-R^{14}$;

or when either Y is independently selected from -O- and - NR^6 -, then together R^1 and R^1 are -alkylene-S-S-alkylene- to form a cyclic group, or together R^1 and R^1 are

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wherein

a) V is selected from the group of aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkynyl and 1-alkenyl;

Z is selected from the group of $-\text{CHR}^2\text{OH}$, $-\text{CHR}^2\text{OC}(\text{O})\text{R}^3$, $-\text{CHR}^2\text{OC}(\text{S})\text{R}^3$, $-\text{CHR}^2\text{OC}(\text{S})\text{OR}^3$, $-\text{CHR}^2\text{OC}(\text{O})\text{SR}^3$, $-\text{CHR}^2\text{OCO}_2\text{R}^3$, $-\text{OR}^2$, $-\text{SR}^2$, $-\text{CHR}^2\text{N}_3$, $-\text{CH}_2\text{aryl}$, $-\text{CH}(\text{aryl})\text{OH}$, $-\text{CH}(\text{CH}=\text{CR}^2_2)\text{OH}$, $-\text{CH}(\text{C}=\text{CR}^2)\text{OH}$, $-\text{R}^2$, $-\text{NR}^2_2$, $-\text{OCOR}^3$, $-\text{OCO}_2\text{R}^3$, $-\text{SCOR}^3$, $-\text{SCO}_2\text{R}^3$, $-\text{NHCOR}^2$, $-\text{NHCO}_2\text{R}^3$, $-\text{CH}_2\text{NHaryl}$, $-(\text{CH}_2)_p\text{-OR}^{19}$, and $-(\text{CH}_2)_p\text{-SR}^{19}$; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group, optionally containing 1 heteroatom, said cyclic group is fused to an aryl group at the beta and gamma position to the Y adjacent to V; or

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl; or

W and W' are independently selected from the group of -H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl and 1-alkynyl and $-\text{R}^9$; or

together W and W' are connected via an additional 2-5 atoms to form a cyclic group, optionally containing 0-2 heteroatoms, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

b) V², W² and W'' are independently selected from the group of -H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl;

Z² is selected from the group of $-\text{CHR}^2\text{OH}$, $-\text{CHR}^2\text{OC}(\text{O})\text{R}^3$, $-\text{CHR}^2\text{OC}(\text{S})\text{R}^3$, $-\text{CHR}^2\text{OCO}_2\text{R}^3$, $-\text{CHR}^2\text{OC}(\text{O})\text{SR}^3$, $-\text{CHR}^2\text{OC}(\text{S})\text{OR}^3$, $-\text{CH}(\text{aryl})\text{OH}$, $-\text{CH}(\text{CH}=\text{CR}^2_2)\text{OH}$, $-\text{CH}(\text{C}=\text{CR}^2)\text{OH}$, $-\text{SR}^2$, $-\text{CH}_2\text{NHaryl}$, $-\text{CH}_2\text{aryl}$; or

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together V^2 and Z^2 are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 ring atoms, optionally containing 1 heteroatom, and substituted with hydroxy, acyloxy, alkyleneoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from a Y attached to phosphorus;

c) Z' is selected from the group of $-OH$, $-OC(O)R^3$, $-OCO_2R^3$, and $-OC(O)SR^3$;

D' is $-H$;

D'' is selected from the group of $-H$, alkyl, $-OR^2$, $-OH$, and $-OC(O)R^3$;

each W^3 is independently selected from the group consisting of $-H$, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl;

p is an integer 2 or 3;

with the provisos that:

a) V , Z , W , W' are not all $-H$ and V^2 , Z^2 , W^2 , W'' are not all $-H$; and

R^2 is selected from the group consisting of R^3 and $-H$;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

each R^4 is independently selected from the group consisting of $-H$, alkylene, $-alkylenearyl$ and aryl, or together R^4 and R^4 are connected via 2-6 atoms, optionally including one heteroatom selected from the group consisting of O, N, and S;

R^6 is selected from the group consisting of $-H$, lower alkyl, acyloxyalkyl, aryl, aralkyl, alkyleneoxycarbonyloxyalkyl, and lower acyl, or together with R^{12} is connected via 1-4 carbon atoms to form a cyclic group;

R^7 is lower R^3 ;

each R^9 is independently selected from the group consisting of $-H$, alkyl, aralkyl, and alicyclic, or together R^9 and R^9 form a cyclic alkyl group;

R^{11} is selected from the group consisting of alkyl, aryl, $-NR^2_2$, and $-OR^2$; and

each R^{12} and R^{13} is independently selected from the group consisting of H, lower alkyl, lower aryl, lower aralkyl, all optionally substituted, or R^{12} and R^{13} together are connected via a chain of 2-6 atoms, optionally including 1 heteroatom selected from the group consisting of O, N, and S, to form a cyclic group;

each R^{14} is independently selected from the group consisting of $-OR^{17}$, $-N(R^{17})_2$,

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Patent
45198.00042.RCE $-\text{NHR}^{17}$, $-\text{SR}^{17}$, and $-\text{NR}^2\text{OR}^{20}$;

R^{15} is selected from the group consisting of $-\text{H}$, lower aralkyl, lower aryl, lower aralkyl, or together with R^{16} is connected via 2-6 atoms, optionally including 1 heteroatom selected from the group consisting of O, N, and S;

R^{16} is selected from the group consisting of $-(\text{CR}^{12}\text{R}^{13})_n-\text{C}(\text{O})-\text{R}^{14}$, $-\text{H}$, lower alkyl, lower aryl, lower aralkyl, or together with R^{15} is connected via 2-6 atoms, optionally including 1 heteroatom selected from the group consisting of O, N, and S;

each R^{17} is independently selected from the group consisting of lower alkyl, lower aryl, and lower aralkyl, or together R^{17} and R^{17} on N is connected via 2-6 atoms, optionally including 1 heteroatom selected from the group consisting of O, N, and S;

R^{18} is selected from the group consisting of $-\text{H}$ and lower R^3 ;

R^{19} is selected from the group consisting of $-\text{H}$, and lower acyl;

R^{20} is selected from the group consisting of $-\text{H}$, lower R^3 , and $-\text{C}(\text{O})-(\text{lower } \text{R}^3)$;

n is an integer from 1 to 3;

with the provisos that:

- 1) when X^3 , X^4 , or X^5 is N, then the respective J^3 , J^4 , or J^5 is null;
- 2) when G^2 , G^3 , or G^4 is O or S, then the respective J^2 , J^3 , or J^4 is null;
- 3) when G^3 or G^4 is N, then the respective J^3 or J^4 is not halogen or a group directly bonded to G^3 or G^4 via a heteroatom;
- 4) if both Y groups are $-\text{NR}^6-$, and R^1 and R^1 are not connected to form a cyclic phosphoramidate, then at least one R^1 is $-(\text{CR}^{12}\text{R}^{13})_n-\text{C}(\text{O})-\text{R}^{14}$;
- 5) R^1 can be selected from the lower alkyl only when the other YR^1 is $-\text{NR}^6-\text{C}(\text{R}^{12}\text{R}^{13})_n-\text{C}(\text{O})-\text{R}^{14}$;

and pharmaceutically acceptable prodrugs and salts thereof.

REMARKS

The Applicants again wish to thank the Examiner for his courtesy during the telephonic interview conducted on November 20, 2002. At the Examiner's request, the Applicants have summarized the contents of that interview and enclose a copy of the Summary herewith. Applicants also wish to thank the Examiner for his consideration of the prior response and arguments and removal of the indefiniteness rejections of point 9 and point 11 of the Office Action dated May 14, 2002.